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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/296,264	04/22/1999	JIM A. WRIGHT	032396-043	8152

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EXAMINER	
SCHMIDT, MARY M	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/296,264	WRIGHT ET AL.	
	Examiner	Art Unit	
	Mary M. Schmidt	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 April 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *27* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on March 19, 2002, for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/296,264 is acceptable and a CPA has been established. An action on the CPA follows.

Drawings

2. The drawing informalities noted in Paper No. 8, mailed on 09-28-00, PTO-948, must now be corrected. Correction can only be effected in the manner set forth in the above noted paper.

Information Disclosure Statement

3. References AJ, AK, and AL have not been considered in the IDS filed 11-29-02 since they are duplicates of the references cited in the notice of references cited (PTO-892) in the Office action mailed 09-28-00.

Election/Restriction

4. Applicant's election with traverse of Group I, claims 1-30, including SEQ ID NO:33, and further SEQ ID NOS:1, 2, 3, 5, 6, 8, 9, 10, 11 and 12, in Paper No. 26, filed 10/8/02, is acknowledged.

The traversal is on the ground(s) that the antisense oligonucleotides directed to human neuropilin gene, mouse neuropilin gene and rat neuropilin gene are not "independent"subjects as defined in MPEP 802.01. Applications state that "[s]uch antisense oligonucleotides are connected in design (i.e. they are selected according to specific disclosed criteria... in operation (i.e. they are capable of binding to the target neuropilin gene sequence...)... and in effect (i.e. they inhibit neuropilin gene expression...). Applicant asserts that claims 1-30, directed to antisense oligonucleotides to human, mouse and rat neuropilin genes, compositions comprising the antisense oligonucleotides are thus related and form a single invention." This is not found persuasive because each of the target gene sequences is patentably distinct as per MPEP 803.04 which states: "Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions with the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq." Therefore, compounds which target different target gene sequences constitute patentably distinct sequences.

Applicant further states that "Groups I, II and III are connected by a single, searchable unifying relationship (i.e. antisense oligonucleotides that inhibit neuropilin gene expression). In view of this single, searchable unifying relationship, Applicants submit that the Examiner would not be seriously burdened by searching and examining the claims of these groups in a single

application." This is not found persuasive for the reasons argued above. Each target nucleic acid is an independent and distinct nucleic acid from which to design patentably distinct antisense nucleic acids.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-25 and 27-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-25 are drawn to compositions and methods comprising antisense nucleic acids to any human or rodent neuropilin gene. Applicant's elected the human gene sequence of instant SEQ ID NO:33 for examination on the merits. The specification as filed does not provide any other target gene sequences for human neuropilin. The nucleic acid sequence of the target nucleic acid is considered "essential material" (MPEP 608.01(p)(I)(A)) for the design of antisense to human neuropilin. Since the specification has not provided a representative number

of species of any other human neuropilin, one of skill in the art would not have recognized that applicant was in possession of a representative number of species of any antisense to other human neuropilin gene sequences. The claims are thus only adequately described for the design of antisense to instant SEQ ID NO:33.

Furthermore, claims 5-22 and 27-30 are drawn to methods of use of antisense to neuropilin in a whole organism for treatment functions and pharmaceutical compositions having implied *in vivo* use in treatment.

MPEP 2163 teaches the following conditions for the analysis of the claimed invention at the time the invention was made in view of the teachings of the specification and level of skill in the art at the time the invention was made:

> The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence....A lack of written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process....Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement....The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

In the instant case, claims 5-22 and 27-30 are not considered adequately described by the specification as filed since the specification as filed does not provide via specific sequence structure a representative number of species of antisense oligonucleotides to human neuropilin gene, elected SEQ IDNO:33, having a specific correlation or nexus to the claimed treatment functions in a whole organism. Note the teachings of the references cited below in regards to the lack of predictability in the art for discernment of antisense function *in vivo* from the antisense nucleic acid structure and the lack of correlation between results *in vitro* and results *in vivo*. Although the specification as filed taught the use of the specific antisense GT13602 on HT-29 tumor growth in CD-1 nude mice, this is not considered a representative number of species of any neuropilin gene antisense for inhibiting the growth or metastasis of any human tumor, or for inhibiting neovascularization. One of skill in the art would not have recognized that applicant was in possession of a representative number of species of antisense to human neuropilin at the time the invention was made.

Response to Arguments

7. Applicant's arguments filed 4/29/02 have been fully considered but they are not persuasive.

Applicants' response is not applicable to the new grounds of rejection stated above.

8. Claims 5-22 and 27-30 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising the claimed antisense of claims 5 and 27 where the claims do not contain the word "pharmaceutical" in the preamble; methods of administering the claimed antisense to neuropilin in cells in cell culture (*in vitro*) with the exception of the antisense GT3602 administered to mice for the inhibition of tumor growth, does not reasonably provide enablement for "pharmaceutical compositions" of antisense to neuropilin, nor methods of administering the claimed antisense *in vivo* for the claimed treatment effects: inhibition of tumor growth, metastasis of a tumor, or inhibition of neovascularization. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification as filed teaches design of SEQ ID NOS:1-30 to the human neuropilin gene (instant SEQ ID NO:33) and administration of the antisense to cancer cells in cell culture. The specification further taught administration of the antisense oligonucleotide GT13602 to CD-1 nude mice with human colon cancer. (See pages 40-44 of the specification.)

There is a high level of unpredictability known in the antisense art for therapeutic, *in vivo* (whole organism) applications. The factors considered barriers to successful delivery of antisense delivery to the organism are: (1) penetration of the plasma membrane of the target cells to reach the target site in the cytoplasm or nucleus, (2) withstanding enzymatic degradation, and (3) the ability to find and bind the target site and simultaneously avoid non-specific binding

(see Branch). Note also Ma et al. who teach (on page 167) that "to gain therapeutic advantage using antisense-based technology, ODNs must have certain characteristics. They must be resistant to degradation, internalize efficiently, hybridize in a sequence specific manner with the target nucleic acid, display adequate bioavailability with a favorable pharmacokinetic profile and be nontoxic." Despite the synthesis of more resilient, nuclease resistant, oligonucleotide backbones and isolated successes with antisense therapy *in vivo*, the majority of designed antisense molecules still face the challenge of successful entry and localization to the intended target and further such that antisense and other effects can routinely be obtained. Flanagan teaches, "oligonucleotides (*in vivo*) are not distributed and internalized equally among organs and tissues.... Unfortunantly, therapeutically important sites such as solid tumors contain very little oligonucleotide following intravenous injections in animals (page 51, column 2)." Ma et al. supports the difficulties of *in vivo* use of ODNs on pages 160-172. Jen et al. further taught that "given the state of the art, it is perhaps not surprising that effective and efficient clinical translation of the antisense strategy has proven elusive. While a number of phase I/II trials employing ONs have been reported..., virtually all have been characterized by a lack of toxicity but only modest clinical effects." (Page 315, col. 2) Green et al. summarizes that "the future of nucleic acid therapeutics using antisense ODNs ultimately depends on overcoming the problems of potency, stability, and toxicity; the complexity of these tasks should now be apparent. Improvements in delivery systems and chemical modifications may lead to safer and more efficacious antisense compounds with improved pharmacokinetics and reduced toxicities." (P.

103, col. B) Note also some of the major outstanding questions that remain in the art taught by Agrawal et al. On page 79, col. 2.

In vitro, antisense specificity to its target may be manipulated by "raising the temperature or changing the ionic strength, manipulations that are commonly used to reduce background binding in nucleic acid hybridization experiments." (Branch, p. 48) Note also Ma et al. who teach that "*in vitro* subcellular distribution is dependent on the type of ODN modification, cellular system and experimental conditions. ODNs, once internalized, are distributed to a variety of subcellular compartments." (Page 168) Discovery of antisense molecules with "enhanced specificity" *in vivo* requires further experimentation for which no guidance is taught in the specification. Note Branch who teaches the state of the art for designing an antisense which inhibits a target *in vivo:* it "is very difficult to predict what portions of an RNA molecule will be accessible *in vivo*, effective antisense molecules must be found empirically by screening a large number of candidates for their ability to act inside cells (Branch, p.49)." Note Jen et al. who teach that "although mRNA targeting is impeccable in theory, many additional considerations must be taken into account in applying these strategies in living cells including mRNA site selection, drug delivery and intracellular localization of the antisense agent." (Abstract) Bennett et al. further taught that "although the antisense paradigm holds great promise, the field is still in its early stages, and there are a number of key questions that need to be answered and technical hurdles that must be overcome....The key issues concerning this class of chemicals center on whether these compounds have acceptable properties as drugs. These include pharmacokinetic,

pharmacological and toxicological properties." (Page 13) As argued above, these issues remain unpredictable in the art for antisense oligonucleotide administration *in vivo*.

Furthermore, although the specification as filed provides by way of example, administration of one antisense to CD-1 nude mice, these experiments do not correlate to a teaching of how to make and use the breath of claimed antisense for the breath of treatment methods claimed. As argued above, each antisense must be considered on an antisense-by-antisense basis for use *in vivo* due to the high level of unpredictability for the factors taught above. Administration of an antisense to a mouse does not provide a teaching of how to make and use the same antisense in other mammals, such as human, unless there is a direct teaching of an expectation of success for the demonstrated physiological effects in both the mouse and in a human. The instant specification as filed does not provide a teaching of how GT13602 may be representative of use in any mammal for the demonstrated physiological effects *in vivo*. It was known in the art that mouse models are not necessarily predictive of results in humans. Note Sigmund et al. who taught the problems in transgene, knock-out and gene-targeted models. Since the goal of antisense technology is to down-regulate a specific gene, the use of the mouse for antisense studies of diseases raises analogous issues to those raised by Sigmund and others. Sigmund states in the first para. That "it should not come as a surprise that many of the phenotypes examined in transgenic and knockout models are influenced by the genetic background in which they are studied. Genetic background is the collection of all genes present in an organism that influences a trait or traits. These genes may be part of the same biochemical

or signaling pathway or of an opposing pathway or may appear unrelated to the gene being studied. Although all mouse strains contain the same collection of genes, it is allelic variation (sequence differences) and the interactions between allelic variants that influence a particular phenotype. These "epigenic" effects can dramatically alter the observed phenotype and therefore can influence or alter the conclusions drawn from experiments." These effects are relevant to the use of mice to study the use of the instantly claimed antisense for the instantly claimed methods of treatment, since they are problematic barriers in many types of murine models used.

Other problems with use of murine models for the study of antisense effects on disease are found when there is no one murine model indicative of a particular type of disease in other mammals such as human. Note the teachings of Blackshear et al. on the problems of using rodent models for the study of mammary gland carcinogenesis. She taught on pages 105-106 that "[a]nimal models of spontaneous and chemically induced mammary gland carcinogenesis have provided some insight into the pathogenesis of breast cancer but do not faithfully mimic the pathology or biological behavior of human breast cancer.... there is no single model that best mimics the pathology and mechanistic deregulation seen in breast cancer. Each model provides a small portion of the puzzle, which helps to clarify the complex interactions associated with the heterogeneous population of cells in the normal mammary gland. These models enable the researcher to examine individual or combinations of perturbations that lead to the initiation and progression of breast cancer." Thus, absent use of an art recognized mouse model of human disease, the art teaches a high level of unpredictability for the correlation of specific treatment

results in mice with an expectation of success of the equivalent effects in humans. In the instant case, although the specification teaches some treatment of colon cancer cells in mice with one specific antisense, such results do not provide an expectation of success to make and use other antisense for treatment of any tumor, metastasis or neovascularization as broadly claimed.

One of skill in the art would not accept on its face the successful delivery of the disclosed antisense molecules *in vivo* (other than GT13602 in mice) and further, treatment effects, in view of the lack of guidance in the specification and the unpredictability in the art. Neither the specification nor technology today teach general guidelines for successful delivery or treatment effects of antisense molecules in whole organisms. Specifically the specification does not teach (1) stability of the antisense molecule *in vivo*, (2)effective delivery to the whole organism and specificity to the target tissues, (3) dosage and toxicity, nor (4) entry of molecule into cell and effective action therein marked by visualization of the desired treatment effects. These key factors are those found to be highly unpredictable in the art as discussed *supra*. The lack of guidance in the specification as filed for these factors would therefore require "trial and error" experimentation beyond which is taught by the specification as filed. Therefore, it would require undue experimentation to practice the invention as claimed.

Response to Arguments

9. Applicant's arguments filed 4/29/02 have been fully considered but they are not persuasive.

Applicants' state on page 9 of the response filed 4/29/02 that "a worker skilled in the art, having regard to the present Specification, would not require undue experimentation in order to design and use antisense oligonucleotides against a human or rodent neuropilin gene. The experimental evidence provided in Examples 3 and 4 of the present application is such that a worker skilled in the relevant art would be convinced that the claimed antisense oligonucleotides would be useful in the treatment of cancer cells in a whole organism...."

However, the newly cited references cast doubt on Applicants assertions since they provide teachings of the high level of unpredictability in the art for the use of any antisense oligonucleotide *in vivo*, and further, the lack of correlation in the art between mice and humans for cancer. As argued above, the amount of experimentation required by one of skill in the art at the time the invention was made would have been undue to make and use the breath of antisense claimed for the claimed treatment effects *in vivo*.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 1, 3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by EST database AA048244.

EST database AA048244 taught an oligonucleotide of 37 bases corresponding to bases 1827-1863 of instant SEQ ID NO:33, with a one base mismatch. Claim 1 is a composition claim drawn to any antisense oligonucleotide or analog thereof from about 7 to about 100 nucleotides in length comprising a sequence complementary to a transcribed region (herein interpreted as the mRNA region, therefore the complementary sequence is the same as the gene coding sequence of instant SEQ ID NO:33). Absent evidence to the contrary, the sequence of EST database AA048244, in view of MPEP 2112.01 ("Wherein the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially

identical processes, a *prima facie* case of either anticipation or obviousness has been established."), the sequence of EST database AA048244 would have the claimed antisense functions. The sequence also contains sequences not complementary to instant SEQ ID NO:33, and thus meets the added limitation of claim 3. Claim 5 is included in the instant rejection because the preamble "pharmaceutical" for the purposes of this prior art rejection is not considered to breath further life and meaning into what was already a known composition.

12. Claims 1, 3, 5, 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by WO9507994/ N Geneseq database accession no. AAQ86161.

WO9507994/ N Geneseq database accession no. AAQ86161 taught an oligonucleotide of 21 bases corresponding to bases 2-16 of instant SEQ ID NO:5, with a one base mismatch. Claim 1 is a composition claim drawn to any antisense oligonucleotide or analog thereof from about 7 to about 100 nucleotides in length comprising a sequence complementary to a transcribed region and claim 26 specifies that the target is instant SEQ ID NO:33. Absent evidence to the contrary, the sequence of WO9507994/ N Geneseq database accession no. AAQ86161, in view of MPEP 2112.01 ("Wherein the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established."), the sequence of WO9507994/ N Geneseq database accession no. AAQ86161 would have the claimed antisense functions due to its high homology with instant SEQ ID NO:5, an antisense to instant SEQ ID

NO:33. The sequence also contains sequences not complementary to instant SEQ ID NO:33, and thus meets the added limitation of claim 3. Claims 5 and 27 are included in the instant rejection because the preamble "pharmaceutical" for the purposes of this prior art rejection is not considered to breath further life and meaning into what was already a known composition.

13. Claims 1, 3, 5, 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by EP0128733/ GenEmbl database accession no. I04090.

EP0128733/ GenEmbl database accession no. I04090 taught an oligonucleotide of 21 bases corresponding to bases 1-18 of instant SEQ ID NO:17, with a three base mismatch. Claim 1 is a composition claim drawn to any antisense oligonucleotide or analog thereof from about 7 to about 100 nucleotides in length comprising a sequence complementary to a transcribed region and claim 26 specifies that the target is instant SEQ ID NO:33. Absent evidence to the contrary, the sequence of EP0128733/ GenEmbl database accession no. I04090, in view of MPEP 2112.01 ("Wherein the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established."), the sequence of EP0128733/ GenEmbl database accession no. I04090 would have the claimed antisense functions due to its high homology with instant SEQ ID NO:17, an antisense to instant SEQ ID NO:33. The sequence also contains sequences not complementary to instant SEQ ID NO:33, and thus meets the added limitation of claim 3. Claims 5 and 27 are included in the instant rejection because the

preamble "pharmaceutical" for the purposes of this prior art rejection is not considered to breath further life and meaning into what was already a known composition.

14. Claims 1, 3, 5, 26 and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6,391,311, SEQ ID NO:6.

U.S. Patent 6,391,311, SEQ ID NO:6 taught an oligonucleotide of 20 bases corresponding to bases 2-16 of instant SEQ ID NO:28, with a one base mismatch. Claim 1 is a composition claim drawn to any antisense oligonucleotide or analog thereof from about 7 to about 100 nucleotides in length comprising a sequence complementary to a transcribed region and claim 26 specifies that the target is instant SEQ ID NO:33. Absent evidence to the contrary, the sequence of U.S. Patent 6,391,311, SEQ ID NO:6, in view of MPEP 2112.01 ("Wherein the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established."), the sequence of U.S. Patent 6,391,311, SEQ ID NO:6 would have the claimed antisense functions due to its high homology with instant SEQ ID NO:28, an antisense to instant SEQ ID NO:33. The sequence also contains sequences not complementary to instant SEQ ID NO:33, and thus meets the added limitation of claim 3. Claims 5 and 27 are included in the instant rejection because the preamble "pharmaceutical" for the purposes of this prior art rejection is not considered to breath further life and meaning into what was already a known composition.

The prior art did not teach the specific antisense of SEQ ID NOS:1-30, nor other antisense to neuropilin with modified linkages, in vectors, in pharmaceutical compositions or for use in methods of inhibiting neuropilin in cells as claimed in instant claims 2, 4, 6-25 and 28-30.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt
December 28, 2002